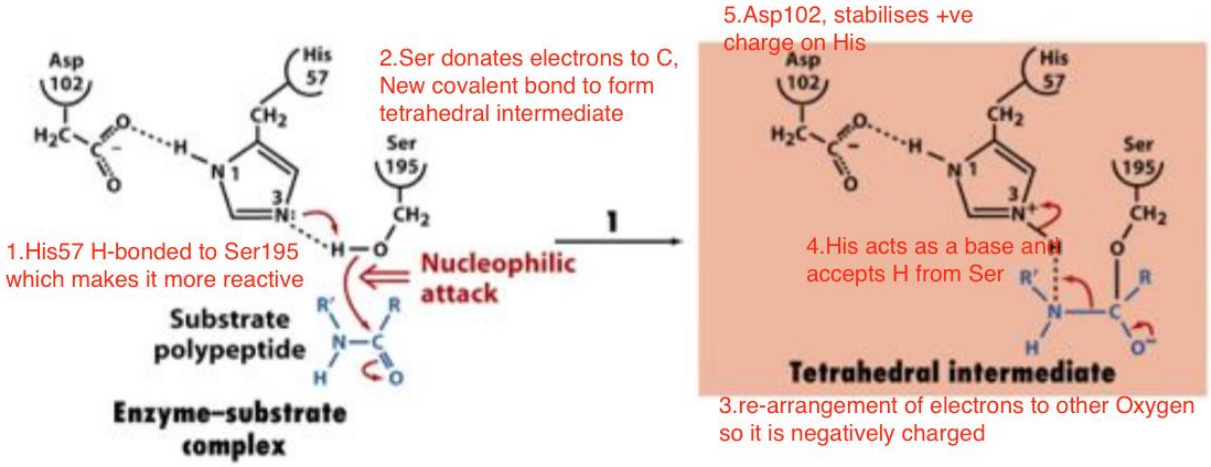
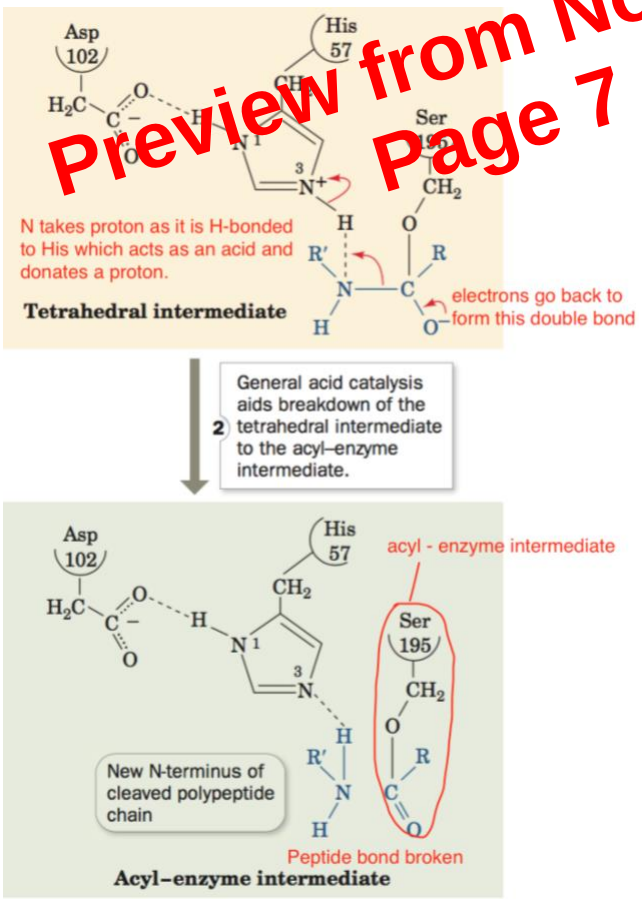
- His57 acid-base catalysis, pKa closes to physiological pH, readily loses and accepts proton
- Asp102 negatively charged, hydrogen bonding

1. Step 1: Nucleophilic attack and general base catalysis
   carbonyl carbon not stable as it is attached to 3 electrons taking groups



2. Step 2: General acid catalysis aids breakdown of tetrahedral intermediate to acyl-enzyme intermediate. Amine product released



- Molecular recognition changed by altering shape (more complementary) /chemical properties of binding surface (phosphorylation)

- Growth factor signalling: RTK > SH2 binds to phosphotyrosine > Gp > kinase cascade > transcription

- Epidermal GF receptor – ligand induced dimerization

    - Cell survival, growth, proliferation, differentiation, inductive signal in development
    - Domain 2 has beta hairpin that interacts with domain 4
    - Ligand binding rotates 1 and 3; join to form EGF binding site
    - New surface exposed on 2 – beta hairpin interacts with domain 2 on another monomer
    - Asymmetric, only 1 kinase active, phosphorylates both tails
    - Grb2 (adapter protein that couples domains) has SH2 that binds to activated receptor.
        - SH2 has 2nd domain for side chains for specificity
    - Brings Sos – nucleotide exchange factor, to receptor
        - Hydrophobic aromatic residues on SH3 binds left-handed poly-proline helix
    - Sos changes the conform of Ras (GTPase) in switch 1 or 2 forms H-bonds with gamma-P
        - H-bonds and electrophilic interactions
        - Lever opens nucleotide binding site > Arg inserted by GAP, glutamine does catalysis
        - releases GDP > binds GTP so becomes activated
    - Ras binds to Raf: form intermolecular beta sheet, extends anti-p sheets in both
        - H-bonds and ionic.
        - Raf doesn't detect GTP
        - Ras displaces N-terminal region to activate kinase phosphorylates Ser+Thr SC